UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,097	06/14/2001	Anton Wellstein	38596.0005	3830

25227 7590 09/16/2004

MORRISON & FOERSTER LLP
1650 TYSONS BOULEVARD
SUITE 300
MCLEAN, VA 22102

EXAMINER	
NICHOLS, CHRISTOPHER J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,097	WELLSTEIN, ANTON	
	Examiner	Art Unit	
	Christopher J Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-17,21-23 and 69-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-17,21-23 and 69-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *10-17,21-23 and 69-94* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7.20.04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Response and Amendment filed 26 July 2004 has been received and entered in full.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

3. The Objection to the Drawings as set forth at pp. 4 ¶6 in the previous Office Action (26 April 2004) is hereby *withdrawn* in view of Applicant's arguments (26 July 2004).

4. The Objection to the Claims as set forth at pp. 4-5 ¶7 in the previous Office Action (26 April 2004) is hereby *withdrawn* in view of Applicant's amendments (26 July 2004).

5. The Rejection of claims **10, 11, 12,** and **21** under 35 U.S.C. 102(b) as set forth at pp. 13-14 ¶26-28 in the previous Office Action (26 July 2004) is hereby *withdrawn* in view of Applicant's amendments (26 July 2004).

Maintained Objections And/Or Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims **80, 81, 90, 91, 93,** and **94** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. No reference sequence is provided in the Specification. As such, the metes and bounds of the residues numbers cannot be determined.

7. Claims **10-17, 21-23,** and **69-94** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *the recombinant human pleiotrophin receptor protein ALK comprising one or more but not all regions selected from the group consisting of an extracellular domain (ECD), an intracellular domain (ICD), a pleiotrophin binding site, a transmembrane domain, and combinations thereof as well as compositions thereof*, does not reasonably provide enablement for *other variants, fragments, domains, or peptido-mimetics as well as compositions thereof.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make** or **use** the invention commensurate in scope with these claims for the reasons as set forth at pp. 5-10 ¶8-16 in the previous Office Action (26 July 2004).

8. Applicant traversed the rejection of the claims on the following grounds: **(a)** the claims are drawn to a human pleiotrophin receptor polypeptide, **(b)** the claims do not require a prediction of identity and function of any given pleiotrophin, and **(c)** the claims do not require a predication of protein structure to ascertain the function of the protein.

9. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons

10. On "**(a)**", the claims as instantly presented are drawn to a recombinant polypeptide comprising one or more but not all regions of a full-length human pleiotrophin receptor protein. The Specification teaches that the human pleiotrophin receptor (ALK) is composed of three

principal regions, an extracellular domain (ECD), a transmembrane region (TM), and an intracellular domain (ICD) (Figure 1A). ALK binds pleiotrophin (PTN) (pp. 9-10). The Specification also teaches that the pleiotrophin binding domain lies within residues 368-447 of the human pleiotrophin receptor protein (pp. 14).

11. However, the specification fails to provide any guidance for the successful isolation and characterization of all species of pleiotrophin receptor and other domains besides extracellular domain (ECD), an intracellular domain (ICD), a pleiotrophin binding site, a transmembrane domain, or peptido-mimetics. Thus the claims are still too broad to be fully supported by the Specification as filed.

12. While pleiotrophin receptors which have the claimed domains may constitute a fecund ground for investigation, the CAFC ruled in *Genentech Inc. v. Novo Nordisk A/S* (CA FC) **42 USPQ2d 1001** (1997) that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Citing *Brenner v. Manson,* **383 U.S. 519, 536, 148 USPQ 689, 696** (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the CFAC stated that tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in the instant specification with respect to the pleiotrophin receptors which have the claimed domains other than recombinant human pleiotrophin receptor protein ALK comprising one or more but not all regions selected

from the group consisting of an extracellular domain (ECD), an intracellular domain (ICD), a pleiotrophin binding site, a transmembrane domain, and combinations thereof.

13. On "**(b)**", the discussion of prediction of protein structure are related to the breadth of the claims and the state of the prior art. As instantly presented, the claims are drawn to a recombinant polypeptide comprising one or more, but not all regions of a full-length human pleiotrophin receptor. This includes and is not limited to any recombinant human polypeptide which binds pleiotrophin and lacks some undefined region. As such, the skilled artisan is left the unpredictable task of determining which recombinant human polypeptide which binds pleiotrophin and lacks some undefined region are encompassed by the instant claims. This constitutes a prediction as only one species of this large genus is adequately presented. Thus, although the specification prophetically considers and discloses general methodologies of identifying said domains (or regions); such a disclosure would not be considered enabling since the state of protein biochemistry is highly unpredictable.

14. On "**(c)**", as noted above the claims are broadly construed to include a large ill-defined genus of human pleiotrophin receptors. Meng *et al.* (14 March 2000) "Pleiotrophin signals increased tyrosine phosphorylation of β-catenin through inactivation of the intrinsic catalytic activity of the receptor-type protein tyrosine phosphatase β/ζ." PNAS **97**(6): 2603-2608 teaches that pleiotrophin (PTN) binds to the receptor protein tyrosine phosphatase (RPTP) β/ζ (pp. 2603; Figure 2). Meng *et al.* teaches that the family of RPTPs are single-chain transmembrane proteins with either one or two intracellular tyrosine phosphatase domains, single transmembrane domains, and variable extracellular domains (pp. 2607). However, Meng *et al.* does not teach which domains are sufficient and necessary to bind PTN, or which residues are important to

maintain the biological activity. Thus the skilled artisan is not offered any support to make or use the invention as claimed which requires the deletion of at least one domain while still remaining a PTN binding receptor. While there is no explicit requirement for protein structure to ascertain the function of the protein, a great deal of work and speculation is necessary to fulfill the claims as instantly presented.

15. Further since the claims explicitly state that the claimed protein comprising one but not all regions of a full-length human pleiotrophin receptor, it encompasses derivatives and fragments of pleiotrophin receptor polypeptides. The inherent problem of utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Therefore the claims as instantly presented constitute an invitation to experiment.

16. Claims **10-17, 21-23,** and **69-94** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons as set forth at pp. 10-13 ¶17-25 in the previous Office Action (26 July 2004).

17. Applicant traversed the rejection of the claims on the following grounds: **(a)** all the domains listed in the claims are taught in the Specification, **(b)** all the functions of the claimed protein listed in the claims are taught in the Specification, **(c)** no peptido-mimetic is claimed, and **(d)** *University of Rochester v. G.D. Searle & Co.* case law is not applicable.

18. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

19. First, the Examiner notes that the above was a rejection of the claims not an objection.

20. Secondly, the Examiner notes that the Applicant is enabled and has written description for a recombinant human pleiotrophin receptor protein ALK comprising one or more but not all regions selected from the group consisting of an extracellular domain (ECD), an intracellular domain (ICD), a pleiotrophin binding site, a transmembrane domain, and combinations thereof as well as compositions thereof.

21. On "**(a)**", Applicant has listed the desired domains but not disclosed their nature, structure, or identity. Therefore they are taken to be desired and/or hypothesized domains which may or may not be present in the instantly claimed protein.

22. On "**(b)**", Applicant has listed the desired functions but not disclosed their nature, structure, or identity. Therefore they are taken to be desired and/or hypothesized functions which may or may not be resident in the instantly claimed protein.

23. On "**(c)**", Applicant is mistaken and directed to instantly presented claim 23. Furthermore the art recognizes that "peptido-mimetic" can pertain to chemical entities, peptides, non-peptide compounds, animal tissue extracts, antibody fragments, cyclic peptides, agonists, antagonists, vegetable extracts, cell extracts, synthetic agents, biologically derived substances as well as

proteinaceous substances, known, and unknown compounds. The claims do not require that the peptido-mimetic possess any particular conserved structure, or other distinguishing feature nor does the Specification delineate a peptido-mimetic of any given pleiotrophin receptor protein. Thus, the claims are drawn to a genus of domains that are defined by hypothesized function and unknown structure.

24. On "**(d)**", the instant claims and the claims in dispute in the *University of Rochester v. G.D. Searle & Co.* case law are analogous. In both claim sets, Applicant claims a compound (instantly a polypeptide) where the function and nature are claimed but no such compound (instantly a polypeptide) fulfills the claims.

25. Finally, the Examiner notes that a sequence described only by a functional characteristic without any known or disclosed correlation between that function and the structure of the sequence, is not a sufficient identifying characteristic to satisfy the written description requirement. The instant claims present such an instance where Applicant has only described what is desired but does not evidence material possession of the invention at the time of filing through means of sequence disclosure or detailing of its structure {see MPEP §2163 I(A)}.

Claim Rejections - 35 USC § 102

26. Claims **1-22** and **69-94** rejected under 35 U.S.C. 102(b) as being anticipated by Iwahara *et al.* (30 January 1997) "Molecular Characterization of ALK, a receptor tyrosine kinase expressed specifically in the nervous system." Oncogene **14**(4): 439-449 (**IDS#12**).

27. Iwahara *et al.* teaches the cloning and characterization of a human ALK receptor that included the extracellular and intracellular domains (kinase domain) but lacked a carboxy-

terminal tail thus meeting the limitations of claims 10, 11, 69, 77, 78, 79, and 89 (pp. 440; Figure 2).

28. Iwahara *et al.* teaches a composition of GST-ALK fusion proteins in Freund's complete adjuvant thus meeting the limitations of claims 21, 22, 76, and 88 (pp. 448).

29. The limitations of claims 12-17, 70-75, 82-87 are all described as properties of a pleiotrophin receptor (pp. 3-5 of the instant Specification). Since a compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)), the ALK receptor taught by Iwahara *et al.* is taken by the Examiner to have these properties.

30. The limitations of claims 80, 81, 90, 91, 93, and 94 are not given patentable weight as no sequence is provided for which the amino acid residues can be assigned. As such, the disclosure of a nucleotide and polypeptide sequences in Figure 1 and the nucleotide sequences of Figure 2 are taken by the Examiner to have inherent support to meet these limitations.

Summary

31. No Claims are allowed.

32. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Elizabeth C Kemmerer

CJN
September 13, 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER